The Natural History of Left Ventricular Hypertrophy in Hypertrophic Cardiomyopathy: An Electrocardiographic Study

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SUMMARY The natural history of electrocardiographic left ventricular hypertrophy was assessed in relation to clinical features, treatment with propranolol and prognosis in 100 patients with hypertrophic cardiomyopathy who were followed 5–20 years (mean 8 years). Seventy-one patients received propranolol, 120–800 mg/day (mean 240 mg). At diagnosis, the voltage measurement from SV<sub>1</sub> + RV<sub>5</sub> was 37 ± 20 mm, the R wave in aV<sub>1</sub> was 12 ± 6 mm and the mean frontal plane voltage was 15 ± 10 mm. After 5 years, these values were increased to 43 ± 22 mm (p < 0.0002), 14 ± 6 mm (p < 0.003) and 17 ± 10 mm (p < 0.01), respectively. Neither a left ventricular outflow tract gradient nor propranolol treatment influenced these voltage changes. Twenty patients had an increase of more than 10 mm in SV<sub>1</sub> + RV<sub>5</sub>, which was associated with exertional chest pain (p < 0.006) and death (p < 0.02). Four patients had a decrease of more than 10 mm in SV<sub>1</sub> + RV<sub>5</sub>. Two of these received high-dose propranolol, one 720 mg/day for 12 years and another 800 mg/day for 12 years. No other patient received more than 480 mg of propranolol daily. In hypertrophic cardiomyopathy there is electrocardiographic evidence of progressive hypertrophy, which is associated with poor prognosis and is not influenced by treatment with propranolol in moderate dosage. Regression of hypertrophy is rare and may be related to long-term treatment with high-dose propranolol.

HYPERTROPHIC cardiomyopathy is characterized by a hypertrophied, nondilated left ventricle.1, 2 For the past decade, β-adrenergic blocking agents have been used to treat symptoms. The results of studies in animals suggest that regression of hypertrophy is due to a direct myocardial action of the β blocker,3 but the effect of these agents on myocardial hypertrophy in patients with hypertrophic cardiomyopathy has not been investigated. In this study we assessed serial ECGs to determine the natural history of hypertrophy in hypertrophic cardiomyopathy in relation to clinical features, prognosis and the results of treatment with propranolol.

Methods

Patients

The electrocardiographic features of left ventricular hypertrophy were assessed retrospectively in 100 of 254 patients with hypertrophic cardiomyopathy who were diagnosed and followed at the Royal Postgraduate Medical School. All 100 study patients fulfilled the following criteria: at least five good-quality 12-lead ECGs recorded over the 5 years after diagnosis or myotomy/myectomy, absence of right bundle branch block at diagnosis or after cardiac surgery, mean frontal-plane axis of −60° to +120°, no record of systemic hypertension and normal blood pressure at diagnosis and during follow-up.

The diagnosis of hypertrophic cardiomyopathy was based on typical clinical,4 echocardiographic,5 hemodynamic6 and angiographic7 features. M-mode echocardiography became available in our hospital in 1973. It was performed at diagnosis in 18 patients. Details of our diagnostic echocardiographic criteria have been reported. Briefly, in patients without clinical and hemodynamic evidence of a left ventricular outflow tract gradient, end-diastolic myocardial wall thickness of at least 1.5 cm was required.

Diagnostic hemodynamic and angiographic studies were performed in all patients. Sixty-four had a left ventricular outflow tract gradient of 20 mm Hg or more at rest or upon provocation (at first with isoproterenol infusion, later with amyl nitrate inhalation and the Valsalva maneuver). Thirty-six patients had no left ventricular gradient, but had clinical features consistent with hypertrophic cardiomyopathy and ECG8 or echocardiographic evidence of left ventricular hypertrophy. The mean left ventricular end-diastolic pressure was 19 ± 10 mm Hg (range 5–45 mm Hg).

Sixty patients were male and 40 female. At diagnosis, the patients were 3–64 years old (mean 33 years). Eight had severe dyspnea (New York Heart Association class III or IV), 47 had exertional chest pain and 23 had syncope. Seven patients were in atrial fibrillation.

Seventy-one patients were treated with propranolol (120–800 mg/day, mean 240 mg/day) for at least 4 years during the period of evaluation. None received calcium-antagonist or antiarrhythmic agents. Their resting heart rate was 40–68 beats/min (mean 61 beats/min). Patients who did not receive propranolol had a resting heart rate of 68–96 beats/min (mean 78 beats/min). Myotomy/myectomy was performed in 10 patients within 4 months after diagnosis and in three patients after at least 5 years of medical treatment. During the follow-up of 5–20 years (mean 8 years),
22 patients died: 13 suddenly, three in cardiac failure, three perioperatively after myotomy/myectomy and three from noncardiac events.

Electrocardiography

Five hundred seventy standard 12-lead ECGs were recorded with the patients in the supine position during quiet respiration. Before 1970, a Hewlett-Packard single-channel recorder (model 1511B) was used. Since 1970, two Hewlett-Packard three-channel recorders (1513A and 1515B) have been used. The ECGs were analyzed by one of the authors and the following features were measured: mean frontal-plane axis, R-wave amplitude in standard lead aV1, the amplitude of the dominant monophasic R wave in lead II, III or aVF when the frontal-plane axis exceeded 30°, and precordial voltage, e.g., the sum of the S wave in lead V1 and the R wave in V5. When possible, amplitude measurements were made from five consecutive complexes to minimize beat-to-beat variation produced by respiration. The ECGs were also evaluated for left atrial enlargement and the presence of normal q waves in precordial leads V3 and V6. The ECGs recorded at diagnosis were compared with those obtained after 5 years of follow-up.

During the follow-up, 11 patients had a negative and five a positive, progressive change of axis of greater than 30°. In these patients, a mean frontal-plane QRS voltage was calculated from the dominant monophasic R wave in the frontal plane by simple trigonometry (fig. 1). This calculation provided an assessment of left ventricular hypertrophy that was independent of changes in the frontal-plane axis (but not of anterior or posterior rotation of the heart). Five patients who developed bundle branch block and one who suffered a myocardial infarction were analyzed separately. The electrocardiographic assessment of ventricular hypertrophy was not compared with M-mode echocardiographic measurements of ventricular septal and left ventricular posterior wall thickness, for the majority (71%) of the ECGs were recorded before 1973.

The paired or unpaired t test was used for quantitative comparison of the electrocardiographic voltage at diagnosis and after 5 years. The chi-square test or Fisher's exact test was used to assess the voltage changes in relation to the clinical and hemodynamic features and prognosis of the patients. The relation of the different electrocardiographic criteria of left ventricular hypertrophy was assessed by linear regression analysis.

Results

The mean voltage in SV1 + RV5 at diagnosis was 36.6 ± 20 mm. Forty-five patients fulfilled the Sokolow-Lyon electrocardiographic criteria for left ventricular hypertrophy (SV1 + RV5 > 35 mm). Compared with those who did not fulfill these criteria, both groups had a similar incidence of exertional chest pain. Neither the presence nor the absence of these voltage criteria was associated with symptoms, hemodynamic measurements or prognosis (table 1). Although the mean voltage in SV1 + RV5 at diagnosis was greater (38 ± 20 mm) in the patients who had a left ventricular gradient than in those without (34 ± 19 mm), the difference was not significant. A family history of sudden death with or without documented hypertrophic cardiomyopathy was associated with SV1 + RV5 ≤ 35 mm (p < 0.04).

After 5 years, the mean precordial voltage had increased to 43.4 ± 22 mm (p < 0.0002). The voltage was unchanged in 23 patients and changed by 10 mm or less in 45. The voltage increased by more than 10 mm in 20 patients and decreased by more than 10 mm in four. The changes were progressive in all patients (figs. 2 and 3). Three of the patients whose precordial voltage increased had an axis change of more than 30° (all negative).

At diagnosis, the voltage in SV1 + RV5 in the patients whose voltage subsequently increased was not significantly different from that in patients whose voltage was unchanged at 5 years (fig. 4), but it was significantly less than that in patients whose voltage

![Figure 1](http://circ.ahajournals.org/FIGURE1.jpg)  
**FIGURE 1.** Calculation of the mean frontal-plane QRS voltage. R aV1 = R-wave amplitude in lead aV1; Cos = cosine (adjacent ÷ hypotenuse); θ = mean frontal-plane axis; V = mean frontal-plane QRS voltage.
TABLE 1. The Relation of Electrocardiographic Left Ventricular Hypertrophy to Clinical and Hemodynamic Features at Diagnosis in 100 patients with Hypertrophic Cardiomyopathy

<table>
<thead>
<tr>
<th>Voltage in SV1 + RV5</th>
<th>Exertional chest pain (n) (%)</th>
<th>Severe dyspnea* (n) (%)</th>
<th>Syncope (n) (%)</th>
<th>LVOT gradient† ≥ 20 mm Hg (n) (%)</th>
<th>LVEDP ≥ 12 mm Hg (n) (%)</th>
<th>Family history of sudden death in HCM (n) (%)</th>
<th>Death from HCM (n) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 35 mm (n = 55)</td>
<td>24 (44)</td>
<td>7 (13)</td>
<td>16 (29)</td>
<td>32 (58)</td>
<td>19 (35)</td>
<td>18 (33)</td>
<td>13 (24)</td>
</tr>
<tr>
<td>&gt; 35 mm (n = 45)</td>
<td>22 (49)</td>
<td>1 (2)</td>
<td>8 (18)</td>
<td>33 (73)</td>
<td>15 (33)</td>
<td>7 (16)</td>
<td>6 (13)</td>
</tr>
</tbody>
</table>

*New York Heart Association class III or IV.
†At rest or upon provocation.

Abbreviations: LVOT = left ventricular outflow tract; LVEDP = left ventricular end-diastolic pressure; HCM = hypertrophic cardiomyopathy.

had decreased by more than 10 mm at 5 years (p < 0.05). A summary of the relation of a change in voltage in SV1 + RV5 after 5 years and the clinical and hemodynamic features is presented in table 2.

Exertional chest pain was more common in patients whose voltage increased by more than 10 mm than in those in whom voltage did not change (p < 0.006).

The incidence of syncope, severe dyspnea, left ventricular outflow gradient at rest or upon provocation and elevated left ventricular end-diastolic pressure was similar whether voltage increased or not. The proportion of patients in these two groups who received β-adrenergic blockers was also similar. A voltage increase of more than 10 mm, however, was associated with sudden death or death from cardiac failure (p < 0.02).

Figure 5 shows the relation of age and the voltage in SV1 + RV5 at diagnosis and after 5 years. The mean voltages at diagnosis in the four age groups were not

![Figure 2](http://circ.ahajournals.org/)

**Figure 2.** Progressive increase in the precordial voltage criteria of left ventricular hypertrophy in a patient with hypertrophic cardiomyopathy who received 160 mg of propranolol per day from 1969 to 1971 and 240 mg/day thereafter.

![Figure 3](http://circ.ahajournals.org/)

**Figure 3.** Progressive decrease in the precordial voltage criteria of left ventricular hypertrophy in patient TH, who had hypertrophic cardiomyopathy and received 720 mg of propranolol per day from 1969 to 1975 and 800 mg/day thereafter.
The relation of a Change in Voltage in $SV_1 + RV_5$ and Clinical and Hemodynamic Features in 94 Patients with Hypertrophic Cardiomyopathy

**Table 2.**

<table>
<thead>
<tr>
<th>Voltage in $SV_1 + RV_5$ at 5 years</th>
<th>Increase $&gt; 10$ mm ($n = 20$)</th>
<th>Change $\leq 10$ mm ($n = 70$)</th>
<th>Decrease $&gt; 10$ mm ($n = 4$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>At diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exertional chest pain</td>
<td>15 (75%)</td>
<td>27 (39%)</td>
<td>4 (100%)</td>
</tr>
<tr>
<td>Severe dyspnea*</td>
<td>1 (5%)</td>
<td>7 (10%)</td>
<td>0</td>
</tr>
<tr>
<td>Syncope</td>
<td>4 (25%)</td>
<td>15 (21%)</td>
<td>2 (50%)</td>
</tr>
<tr>
<td>LVEDP $\geq 20$ mm Hg</td>
<td>8 (40%)</td>
<td>22 (31%)</td>
<td>0</td>
</tr>
<tr>
<td>LVOT gradient</td>
<td>14 (70%)</td>
<td>39 (56%)</td>
<td>4 (100%)</td>
</tr>
<tr>
<td>Family history of sudden death ± HCM</td>
<td>3 (15%)</td>
<td>18 (26%)</td>
<td>1 (25%)</td>
</tr>
<tr>
<td>Beta-blocker therapy</td>
<td>13 (65%)</td>
<td>51 (73%)</td>
<td>4 (100%)</td>
</tr>
<tr>
<td>Death from HCM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sudden</td>
<td>4 (25%)</td>
<td>7 (10%)</td>
<td>1 (25%)</td>
</tr>
<tr>
<td>Cardiac failure</td>
<td>2 (10%)</td>
<td>0 (0%)</td>
<td>0</td>
</tr>
<tr>
<td>Surgery</td>
<td>2 (10%)</td>
<td>1 (1%)</td>
<td>0</td>
</tr>
</tbody>
</table>

*New Heart Association class III or IV.

Abbreviations: LVEDP = left ventricular end-diastolic pressure; LVOT = left ventricular outflow tract gradient at rest or upon provocation; HCM = hypertrophic cardiomyopathy.

The mean increase in voltage was greatest in the children, but the increase was significant only in patients 15–30 years old and in those more than 45 years old at diagnosis. The proportions of patients in the four age groups who increased their voltage in $SV_1 + RV_5$ by more than 10 mm were not significantly different.

The changes in the four patients who showed a decrease of more than 10 mm in the precordial voltage were progressive and were not associated with axis shifts or conduction disease (table 3). Patients NS and

**Figure 4.** The relation of the mean precordial voltage at diagnosis, after 5 years and at last follow-up in patients with and those without a change of more than 10 mm in precordial voltage after 5 years.

**Figure 5.** The relation of age at diagnosis and mean precordial voltage at diagnosis and after 5 years in 94 patients with hypertrophic cardiomyopathy.
TH (fig. 3) exhibited a decrease in voltage of 44 mm and 29 mm, respectively, over 12 years. One of these patients received 800 mg and the other 720 mg of propranolol daily during the evaluation period. No other patient received more than 480 mg of propranolol daily.

Forty patients fulfilled one of the criteria for left ventricular hypertrophy (R aV_L > 11 mm); neither this criterion nor the SV_1 + RV_5 > 35 mm criterion correlated with clinical status or any hemodynamic measurement. The mean R-wave amplitude in lead aV_L (11.5 ± 6.3 mm at diagnosis) was significantly increased at 5 years (13.8 ± 5.7 mm, p < 0.003). Sixteen of the 20 patients in whom the precordial voltage increased by more than 10 mm had an increase of more than 3 mm in R-wave amplitude in lead aV_L, whereas such a change was seen in only five other patients (p < 0.03).

Left atrial enlargement was diagnosed in 49 patients and was associated with SV_1 + RV_5 > 35 mm (p < 0.005) and with R aV_L > 11 mm (p < 0.01). At five years, an additional eight patients had this abnormality; in five of these patients, the voltage in SV_1 + RV_5 increased by at least 10 mm.

Sixty-four patients had no q wave in lead V_5 or V_6 at diagnosis. This finding was associated with the presence of the precordial voltage criterion for left ventricular hypertrophy (SV_1 + RV_5 > 35 mm, p < 0.001). The loss of a q wave in lead V_5 or V_6 at 5 years was observed in nine patients and was not associated with a change in frontal-plane axis. Eight of these nine patients also had an increase of at least 10 mm in precordial voltage.

The mean frontal-plane axis at diagnosis was +18.6 ± 43.8°. The frontal-plane axis was normal in 74 patients, ≤ 30° in 19 and > 90° in one. The frontal-plane axis at diagnosis did not correlate with precordial voltage, frontal-plane voltage (assessed in the dominant R wave from leads II, III, aV_L or aV_F) or mean frontal-plane voltage corrected for axis. The precordial voltage criteria of left ventricular hypertrophy were not associated with left-axis deviation (axis ≤ −30°) or an axis of 0° or less (fig. 6).

Table 4 shows the relation of precordial voltage with frontal-plane voltage and mean frontal-plane voltage corrected for axis. There was no correlation between precordial and frontal voltage when the mean frontal-plane axis was less than or equal to −30°; the correlations were modest when the axis was greater than −30°. During follow-up, 11 of 16 patients who had an axis change of more than 30° remained normal, whereas four developed severe left-axis deviation (less than −45°); of these four, one died suddenly and another died in the perioperative period after myotomy/myectomy. In these 16 patients, the change in precordial voltage correlated well with the changes in frontal-plane voltage (r = 0.87, p < 0.001) and mean frontal-plane voltage (r = 0.54, p < 0.05).

During the 5 years after diagnosis, six patients exhibited conduction abnormalities associated with sudden changes in the voltage in SV_1 + RV_5. Two developed right and one left bundle branch block; one suffered a massive anterior myocardial infarction and died in cardiac failure, and another had progressive left-axis deviation and developed right and then left bundle branch block (table 5). An additional patient developed progressive right-axis deviation and incomplete right bundle branch block and died from respiratory failure complicating acute infective polyneuritis. Postmortem examination showed hypertrophic cardiomyopathy predominantly affecting the right ventricle.

**Discussion**

There is a strong correlation between both precordial and frontal-plane electrocardiographic voltage and heart weight in patients with concentric myocardial hypertrophy. In hypertrophic cardiomyopathy, the distribution of myocardial hypertrophy is variable and often asymmetric; the relation of electrocardiographic criteria for left ventricular hypertrophy and heart weight has not been determined. Previous studies have, however, shown an association between electrocardiographic criteria for left ventricular hypertrophy and echocardiographic measurements of myocardial wall thickness. The significance of abnormal q waves, which are present in approximately 30% of patients with hypertrophic cardiomyopathy, is uncertain. Abnormal q waves may be related to septal hypertrophy, premature activation of the base of the septum, altered electrophysiologic properties of the myopathic tissue. In an early study on the natural history of hypertrophic cardiomyopathy, abnormal q waves developed or increased in 12 and disappeared in 11 of 126 patients. The disappearance of abnormal left precordial and limb lead q waves has also been reported in association with progressive hypertrophy of the left ventricu-

![Figure 6. The frontal-plane axis at diagnosis in 94 patients with hypertrophic cardiomyopathy.](http://circ.ahajournals.org/Download/journals/000-000-000-000/1237.png)
TABLE 3. Clinical, Hemodynamic and Electrocardiographic Characteristics of Four Patients with Hypertrophic Cardiomyopathy in Whom the Precordial Voltage Decreased

<table>
<thead>
<tr>
<th>Pt</th>
<th>Age (years)</th>
<th>Exertional chest pain</th>
<th>Dyspnea*</th>
<th>Syncope</th>
<th>LVOT gradient (mm Hg)</th>
<th>LVEDP (mm Hg)</th>
<th>β blocker (mg/day)</th>
<th>ECG at diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH</td>
<td>19</td>
<td>Yes</td>
<td>I</td>
<td>No</td>
<td>Labile</td>
<td>19</td>
<td>240</td>
<td>SR 45 -30°</td>
</tr>
<tr>
<td>NS</td>
<td>28</td>
<td>Yes</td>
<td>II</td>
<td>Yes</td>
<td>Resting</td>
<td>10</td>
<td>800</td>
<td>SR 92 -30°</td>
</tr>
<tr>
<td>EC</td>
<td>52</td>
<td>Yes</td>
<td>II</td>
<td>No</td>
<td>Resting</td>
<td>15</td>
<td>80-200</td>
<td>SR 59 0°</td>
</tr>
<tr>
<td>TH</td>
<td>34</td>
<td>Yes</td>
<td>II</td>
<td>Yes</td>
<td>Resting</td>
<td>16</td>
<td>720-800</td>
<td>AF 65 +30°</td>
</tr>
</tbody>
</table>

*New York Heart Association class III or IV.

Abbreviations: LVOT = left ventricular outflow tract; LVEDP = left ventricular end-diastolic pressure; SR = sinus rhythm; AF = atrial fibrillation; SD = sudden death; HCM = hypertrophic cardiomyopathy.

TABLE 4. The Effect of Axis on the Relation of Precordial Voltage and Frontal Plane Voltage in 94 Patients with Hypertrophic Cardiomyopathy

<table>
<thead>
<tr>
<th>Dominant monophasic R wave in:</th>
<th>At diagnosis</th>
<th>At 5 years</th>
<th>Change in voltage</th>
</tr>
</thead>
<tbody>
<tr>
<td>aVL (axis ≤ -30°)</td>
<td>r = 0.03 NS</td>
<td>r = 0.44 NS</td>
<td>r = 0.10 NS</td>
</tr>
<tr>
<td>aVR (axis &gt; -30°, ≤ +30°)</td>
<td>r = 0.62 p &lt; 0.001</td>
<td>r = 0.45 p &lt; 0.01</td>
<td>r = 0.68 p &lt; 0.001</td>
</tr>
<tr>
<td>aVF, II or III (axis &gt; +30°)</td>
<td>r = 0.68 p &lt; 0.001</td>
<td>r = 0.65 p &lt; 0.001</td>
<td>r = 0.57 p &lt; 0.001</td>
</tr>
<tr>
<td>Mean frontal-plane voltage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>calculated from:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>R aVL (axis ≤ -30°)</td>
<td>r = 0.17 NS</td>
<td>r = 0.16 NS</td>
<td>r = 0.15 NS</td>
</tr>
<tr>
<td>R aVR (axis &gt; -30°, ≤ +30°)</td>
<td>r = 0.56 p &lt; 0.001</td>
<td>r = 0.50 p &lt; 0.01</td>
<td>r = 0.64 p &lt; 0.001</td>
</tr>
<tr>
<td>RaVF, II or III (axis &gt; +30°)</td>
<td>r = 0.70 p &lt; 0.001</td>
<td>r = 0.71 p &lt; 0.001</td>
<td>r = 0.19 NS</td>
</tr>
</tbody>
</table>

The criteria SV₁ + RV₅ > 35 mm and R aVL > 11 mm were used to assess left ventricular hypertrophy. Both are affected by the presence of left-axis deviation. The R-wave amplitude in aVL is accentuated by rotation of the axis superiorly, whereas chest lead voltage is reduced. Thus, there is a stronger correlation between changes in SV₁ + RV₅ and R aVL in patients whose axis was normal than in those who had left-axis deviation (table 4).

The mean frontal-plane voltage should be a more accurate measure of frontal-plane voltage than the dominant R-wave amplitude and should overcome the inaccuracies in assessment of frontal-plane voltage during the time when the frontal axis changes. In this study, use of mean frontal-plane voltage did not improve the correlation with precordial voltage in patients who had left-axis deviation. This finding sug-

TABLE 5. Clinical, Hemodynamic and Electrocardiographic Characterization of Six Patients Who Exhibited Major Changes in Conduction During the 5 Years After Diagnosis

<table>
<thead>
<tr>
<th>Pt</th>
<th>Age (years)</th>
<th>Exertional chest pain</th>
<th>Dyspnea†</th>
<th>Syncope</th>
<th>LVOT gradient (mm Hg)</th>
<th>LVEDP (mm Hg)</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>MB+</td>
<td>15</td>
<td>No</td>
<td>II</td>
<td>No</td>
<td>Resting</td>
<td>25</td>
<td>Beta blockers, diuretics</td>
</tr>
<tr>
<td>MB</td>
<td>25</td>
<td>No</td>
<td>II</td>
<td>No</td>
<td>Labile</td>
<td>12</td>
<td>None</td>
</tr>
<tr>
<td>YZ</td>
<td>25</td>
<td>Yes</td>
<td>II</td>
<td>Yes</td>
<td>Resting</td>
<td>15</td>
<td>Digoxin, β blockers</td>
</tr>
<tr>
<td>VH</td>
<td>47</td>
<td>No</td>
<td>II</td>
<td>Yes</td>
<td>Labile</td>
<td>17</td>
<td>Digoxin, β blockers</td>
</tr>
<tr>
<td>JR</td>
<td>28</td>
<td>No</td>
<td>II</td>
<td>No</td>
<td>Resting</td>
<td>45</td>
<td>Digoxin, β blockers</td>
</tr>
<tr>
<td>AS</td>
<td>8</td>
<td>No</td>
<td>I</td>
<td>No</td>
<td>Resting</td>
<td>20</td>
<td>None</td>
</tr>
</tbody>
</table>

*Postmortem examination showed gross, predominantly right ventricular hypertrophic cardiomyopathy.
†New York Heart Association class III or IV.

Abbreviations: LVOT = left ventricular outflow tract; LVEDP = left ventricular end-diastolic pressure; SR = sinus rhythm; AF = atrial fibrillation; LAH = left atrial hypertrophy; RAD = right-axis deviation; RBBB = right bundle branch block; LBBB = left bundle branch block; MI = myocardial infarction; CCF = cardiac failure; CVA = cerebral vascular accident; SD = sudden death; HCM = hypertrophic cardiomyopathy.
suggests that left-axis deviation in these patients was associated not only with a change in frontal-plane axis, but also with an additional conduction abnormality or change in cardiac position or geometry. Grant\(^{20}\) showed that the left-axis deviation in patients with left ventricular hypertrophy is not due to long-axis rotation (clockwise or counterclockwise), but may be contributed to by superior and posterior bowing of the left ventricle. Our findings and Grant’s observations are consistent with the accentuation of the normal posterior and superior terminal forces in patients with left ventricular hypertrophy, as well as in the majority of those with hypertrophic cardiomyopathy.\(^{21,\ 22}\)

We observed a significant increase in mean precordial and frontal-plane voltage 5 years after diagnosis. A change of more than 10 mm in precordial voltage is unlikely to occur for technical reasons alone.\(^{23}\) When this criterion was applied, 74% of patients showed no evidence of change and 22% exhibited progressive hypertrophy. A 10-mm increase in voltage was associated with exertional chest pain at diagnosis ($p < 0.006$) and sudden death ($p < 0.02$), but not with elevated filling pressure or the presence of a left ventricular gradient. Four patients in whom the precordial voltage did not change by 10 mm developed marked, progressive left-axis deviation and an additional two developed left bundle branch block. One of these six patients died perioperatively and two died suddenly. The hypothesis that development of left bundle branch block is a manifestation of anatomic progression of left ventricular hypertrophy\(^{24,\ 25}\) may help to explain the conduction changes in these patients and in the nine who lost lateral precordial q waves.

Kaltenbach et al.\(^{26}\) reported regression of myocardial hypertrophy in hypertrophic cardiomyopathy during long-term, high-dose verapamil treatment, but these observations have not been confirmed.\(^{27}\) In this study, $\beta$-adrenergic blockers could not be shown to influence hypertrophy. The proportion of patients who received these agents was identical in the group in which precordial voltage increased and the group in which precordial voltage did not change after 5 years. These drugs were given to treat symptoms. Although conclusions about therapeutic efficacy in reducing left ventricular hypertrophy cannot be drawn, resemblances between the actions of propranolol and calcium antagonists on cell function\(^{28}\) should be considered when appraising such reports.\(^{26}\)

Regression of hypertrophy and a decrease in precordial voltage of 10 mm or more occurred in four patients (table 3). Two of these (patients NS and TH) exhibited impressive gradual diminution of voltage that was not attributable to technical factors or changes in frontal-plane axis. Both were receiving high-dose propranolol (800 and 720 mg/day) during the entire evaluation period, whereas no other patient received more than 480 mg/day. Though the depressant side effects of $\beta$ blockers often limit their use in such high doses, fur-

### Table 3. (Continued)

<table>
<thead>
<tr>
<th>Rhythm</th>
<th>SV(_1) + RV(_5) (mm)</th>
<th>Axis</th>
<th>Rhythm</th>
<th>SV(_1) + RV(_5) (mm)</th>
<th>Axis</th>
<th>Comment</th>
<th>Course</th>
<th>Family history</th>
</tr>
</thead>
<tbody>
<tr>
<td>SR</td>
<td>27</td>
<td>+110°</td>
<td>SR</td>
<td>22</td>
<td>+160°</td>
<td>RAD, incomplete RBBB</td>
<td>Death from Guillain-Barre syndrome</td>
<td>HCM + SD</td>
</tr>
<tr>
<td>SR</td>
<td>5</td>
<td>+120°</td>
<td>SR</td>
<td>30</td>
<td>0°</td>
<td>RBBB</td>
<td>Alive</td>
<td>HCM + SD</td>
</tr>
<tr>
<td>SR</td>
<td>53</td>
<td>+80°</td>
<td>AF</td>
<td>25</td>
<td>+40°</td>
<td>MI</td>
<td>Death from CCF</td>
<td>None</td>
</tr>
<tr>
<td>SR</td>
<td>35</td>
<td>+70°</td>
<td>AF</td>
<td>13</td>
<td>+90°</td>
<td>RBBB</td>
<td>Death from CVA</td>
<td>None</td>
</tr>
<tr>
<td>SR</td>
<td>33</td>
<td>-10°</td>
<td>Atrial flutter</td>
<td>20</td>
<td>-15°</td>
<td>LBBB</td>
<td>SD</td>
<td>HCM + SD</td>
</tr>
<tr>
<td>SR</td>
<td>184</td>
<td>0°</td>
<td>SR</td>
<td>93</td>
<td>-60°</td>
<td>Alternating LBBB and RBBB</td>
<td>Alive</td>
<td>None</td>
</tr>
</tbody>
</table>

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ther observations of their effect on hypertrophy are of interest in those who can tolerate these high doses.

In hypertrophic cardiomyopathy, the precise nature of the disease process and its relation to hypertrophy are not understood. Cellular disorganization usually corresponds to areas of increased myocardial thickness, but may be widespread in the ventricular myocardium, without associated hypertrophy. Left ventricular hypertrophy in patients who die suddenly is usually of hypertrophy as interpreted from the ECG, echocardiography was rare and was associated with high-dose propranolol therapy. Hypertrophy may only be a marker, and an imperfect one, for the distribution and extent of disease, and the latter may influence prognosis most. Routine clinical assessment of the distribution of the disease still relies on patterns of hypertrophy as interpreted from the ECG, echocardiogram and angiogram.

In our study, hypertrophy progressed in 22% of patients and was associated with poor prognosis. Regression was rare and was associated with high-dose propranolol therapy. The effect on hypertrophy of any intervention must be assessed in relation to this natural history.

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Circulation. 1982;66:1233-1240
doi: 10.1161/01.CIR.66.6.1233
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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